Notice of Allowability	Application No.	Applicant(s)	
	09/994,701	WILLSON ET AL.	
	Examiner	Art Unit	
	Michael Burkhart	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *the RCE dated 4/21/2009*.

2. ☒ The allowed claim(s) is/are *10-13,16,22-25,29,30,34-46 and 49*.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☒ Interview Summary (PTO-413), Paper No./Mail Date *5/19/2009* .
7. ☒ Examiner's Amendment/Comment
8. ☐ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Richard Willson, Jr. on 5/20/2009.

The application has been amended as follows:

In the claims:

10. [Currently Amended] A method for separating compounds comprising the steps of: contacting a mixture comprising cell lysate or enzyme and a target polynucleotide compound which includes at least four non-shielded purine or pyrimidine moieties, and other compounds, with a solid composition including immobilized metal ions capable of binding compounds containing a non-shielded purine or pyrimidine moiety, to form a liquid product containing a reduced amount of the target polynucleotide; and exposing the solid composition to an elutant which selectively elutes the polynucleotide target compound; and collecting the target compound ~~substantially free of~~ ~~polypeptides~~ substantially free from both protein contaminants and histidine tags.

11. [Currently Amended] The method of claim 10, further comprising the step of: separating the ~~supernatant~~ liquid from the solid composition.

12. [Currently Amended] A method for separating compounds comprising the steps of: passing a mixture of compounds including target polynucleotides comprising at least four non-shielded purine moieties, at least four non-shielded pyrimidine moieties, or mixtures thereof, ~~or~~

~~mixture thereof.,.~~ through a column comprising an IMAC ligand, wherein the ligand is capable of differentially binding the polynucleotides; and
eluting and collecting purified samples of the target polynucleotides substantially free from both protein contaminants and ~~his-tags~~ histidine tags.

Claims 14-15 are not listed in the amendment dated 4/21/2009, but were previously canceled.

16. [Currently Amended] A method for purifying a lysate or enzyme product comprising a crude DNA or RNA target compound containing [[a]] at least four non-shielded purine and/or pyrimidine base moieties, said method comprising the steps of: forming a crude mixture comprising a target compound and contaminants; contacting the crude mixture with an agent including an IMAC ligand capable of binding to the target compound to form an IMAC ligand complex ~~without the presence of his-tags~~;
separating the complex from the contaminants; and
recovering the target compound from the complex substantially free from both protein contaminants and histidine tags.

22. [Currently Amended] A method according to Claim 35 further comprising the steps of: separating the supernatant liquid from the solid composition; or further comprising the steps of: separating the supernatant liquid from the solid composition and
eluting the ~~compounds~~ RNA and/or DNA including a non-shielded purine or pyrimidine moiety from the solid composition.

23. [Currently Amended] A method for separating compounds comprising the step of: contacting a mixture comprising cell lysate or enzyme and a target polynucleotide including a non-shielded purine or pyrimidine moiety and a compound including a shielded purine or pyrimidine moiety with a solid composition including immobilized metal ions capable of binding compounds containing a non-shielded purine or pyrimidine moiety ~~without the presence of his-tags~~ to form a supernatant liquid having a reduced amount of compounds including a non-shielded purine or pyrimidine moiety;

wherein the compound including a non-shielded purine or pyrimidine moiety comprises a single stranded nucleic acid oligomer, or a single stranded nucleic acid polymer and the compounds including a shielded purine or pyrimidine moiety comprise double stranded nucleic acid oligomers or double stranded nucleic acid polymers;
wherein the supernatant liquid ~~and~~ contains less than or equal to 5% by weight compounds comprising a non-shielded purine or pyrimidine moiety and the solid composition is substantially free from both protein contaminants and histidine tags.

25. [Currently Amended] A method of Claim 22 wherein the supernatant liquid comprises compounds including a shielded purine or pyrimidine moiety having less than or equal to [[0.0 I %]] 0.01% by weight compounds which include a non-shielded purine or pyrimidine moiety.

29. [Currently Amended] A method of Claim 23 wherein the mixture comprises poly(A) tailed mRNA sequences and other mRNA sequences from eukaryotic cells, the poly(a) mRNA sequences elute after the other mRNA sequences[[~]] ; or wherein the mixture of compounds comprises denatured nucleic acid sequences, wherein sequences having A-rich regions elute after sequences having T - rich regions, so that complementary strands can be resolved.

30. [Currently Amended] A method of Claim 23 wherein the solution [[ef-]] comprises denatured nucleic acid sequences, wherein sequences having C rich regions elute after sequences having G-rich regions so that complementary strands can be resolved; or wherein the mixture of compounds comprises denatured or partially denatured nucleic acid sequences having A-C, A-G, A-C-G, T-G, T-C and or T-G-C rich regions wherein the sequences having the A-C, A-G, and/or A-C-G rich regions elute after their complementary sequences having T-G, T-C and or T-G-C rich regions resulting in a resolution of complementary sequences.

32. [Canceled]

35. [Currently Amended] A method for separating compounds comprising the step of: contacting

a mixture comprising cell lysate or enzyme comprising double-stranded DNA and additionally comprising RNA and/or DNA, ~~which contains~~ said RNA and/or DNA containing single-stranded portions having a non-shielded purine or pyrimidine moiety, with a solid composition comprising immobilized metal ions capable of binding compounds having a ~~nonshielded~~ non-shielded purine or pyrimidine moiety, to form a supernatant liquid having a reduced amount of RNA and/or DNA having single-stranded portions ~~and substantially free of polypeptides~~ and a solid composition substantially free from both protein contaminants and histidine tags.

36. [Currently Amended] A method for separating compounds comprising the steps of: passing a solution comprising at least one polynucleotide, the polynucleotide containing single-stranded portions having at least four non-shielded purine or pyrimidine moieties through a column including an IMAC ligand,
where the ligand is capable of differentially binding the polynucleotide without the presence of histidine tags ~~his-tags~~;
and collecting purified samples of each polynucleotide compound substantially free from both protein contaminants and histidine tags.

40. [Currently Amended] The method of Claim ~~32~~ 10 wherein the contacting of the crude ~~mixture~~ with the ~~agent~~ solid composition ~~including an IMAC ligand capable of binding to the target compound to form an IMAC ligand complex~~ is performed in batch mode.

41. [Currently Amended] The method of Claim ~~32~~ 10 wherein the target compound comprises RNA having at least four non-shielded purine and/or pyrimidine moieties and is separated from a lysate containing double-stranded DNA.

42. [Currently Amended] The method of Claim ~~32~~ 10 wherein the target compound recovered from the ~~complex~~ solid composition is present in the original mixture at a concentration of less

than [[I]] 1 micromolar.

43. [Currently Amended] The method of Claim ~~32~~ 10 wherein the contacting of the ~~crude~~ mixture with the solid composition ~~agent including an IMAC ligand capable of binding to the target compound to form an IMAC ligand complex in~~ is performed in batch mode, and the target compound ~~recovered from the complex~~ collected is present in the original mixture at a concentration of less than 1 micromolar.

45. [Currently Amended] A method of Claim 10, wherein the target compound comprises DNA. ~~for separating compounds comprising the steps of:~~
~~contacting a mixture comprising cell lysate or enzyme and a DNA target compound which includes at least four non-shielded purine or pyrimidine moieties, and other compounds, with a solid composition including immobilized metal ions capable of binding compounds containing a non-shielded purine or pyrimidine moiety, to form a liquid product containing a reduced amount of the DNA target compound which includes at least four a non-shielded purine or pyrimidine moieties; and collecting the DNA target compound substantially free of polypeptide protein.~~

46. [Currently Amended] A method of Claim 10, wherein the target compound comprises RNA. ~~for separating compounds comprising the steps of: contacting a mixture comprising cell lysate or enzyme and an RNA target compound which includes at least four non-shielded purine or pyrimidine moieties, and other compounds, with a solid composition including immobilized metal ions capable of binding compounds containing a non-shielded purine or pyrimidine moiety, to form a liquid product containing a reduced amount of the RNA compound which includes at least four a non-shielded purine or pyrimidine moieties; and collecting the target compound substantially free of protein.~~

47. [Canceled]

48. [Canceled]

Claims 32, 47 and 48 were canceled to prevent duplicate claiming issues.

The following is an examiner's statement of reasons for allowance: the prior art applied, Petty and Verdine et al. (see, e.g. the Final Office Action dated 1/22/2009) teach the inclusion of histidine tags in proteins (Petty, 1996) or polynucleotides (Verdine et al, WO 98/00435). These molecules are purified via affinity of the histidine tags for an IMAC ligand, and are thus excluded by the instant claims by the recitation that the instant methods are free of protein products (the teachings of Petty are limited to the purification of histidine tagged proteins) and histidine tags (Verdine et al teach modifying polynucleotides via 6-histaminyl purine residues, which are referred to as "histidine tags", or "H6 tags", by the instant specification, Verdine et al, and Min et al (1996, of record)). The remainder of the prior art does not teach or suggest the purification or removal of single-stranded polynucleotides without the use of histidine tags.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Burkhart whose telephone number is (571)272-2915. The examiner can normally be reached on M-F 8AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael Burkhart/
Primary Examiner, Art Unit 1633